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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,014	06/06/2006	Shuchong Pan	07039-409US1	9426

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EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
06/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,014	PAN ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-44* is/are pending in the application.

4a) Of the above claim(s) *11-15 and 17-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-10 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/16/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/5/09, 5/15/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed 1/5/09 is acknowledged. Claims 2-5 are cancelled. Claims 1 and 6-10 are amended. Claims 1 and 6-44 are pending in this application. Claims 11-15, and 17-44 are withdrawn without traverse (the response filed on 5/15/08) from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

2. Claims 1, 6-10 and 16 are under examination with respect to SEQ ID NOs:1, 3 and 36 in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

4. Applicant's arguments filed on 1/5/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Drawings

5. The objection to drawings/figures 1, 2 and 4 is withdrawn in response to Applicant's arguments on p. 12-13 of response.

Specification

6. The objection to the specification is withdrawn in response to Applicant's amendment to the specification.

Claim Rejections/Objections Withdrawn

7. The objection to claims 1-10 and 16 as encompassing non-elected sequences is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 2-5.

The rejection of claims 1 and 16 under 35 U.S.C. 102(b) as being anticipated by U. S. Patent No. 5948761 (Sellhamer et al., issued Sep 7, 1999) is withdrawn in response to Applicant's amendment to the claims.

The rejection of claims 1 and 16 under 35 U.S.C. 102(b) as being anticipated by US. Patent No. 5434133 (Tanaka et al. issued Jul 18, 1995) is withdrawn in response to Applicant's amendment to the claims.

Claim Rejections/Objections Maintained

In view of the amendment filed on 1/5/09, the following rejections are maintained.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-9 and 16 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for a purified polypeptide BNP2 comprising the amino acid sequence of SEQ ID NO: 3 and 36, does not reasonably provide

enablement for a structurally and functionally polypeptide comprising SEQ ID NO:1, 90-95% to SEQ ID NO:1, and their variants at least 85%-95% to a fragment of SEQ ID NO:1 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in the scope with these claims. The rejection is maintained for the reasons made of record.

Claims 1, 6-9 and 16 as amended are directed to a purified polypeptide comprising an amino acid sequence selected from the group consisting of a) the amino acid sequence of SEQ ID NO:1, 3, or 36, b) a sequence having at least seven contiguous residues to the amino acid sequence of SEQ ID NO:1, c) a sequence having at least 85%-95% sequence identity to the amino acid sequence of SEQ ID NO:1 and d) a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length and a pharmaceutical composition comprising the claimed polypeptides.

On p.14-15 of the response, Applicant argues that instant claims are fully enabled because the specification teaches how to make, obtain, use and obtain BNP isoforms and also provides examples 5, 6 and 8-10 (p.8, line 17-p. 9, lin419; p. 11, line 26-p. 12, line 21; p. 12, line 22-p. 13, line10; p. 20, line 29-p. 29, line 18). Applicant also argues that the specification teaches several methods for detecting BNP isoforms and nucleic acids, which may be used to monitor treatment of a patient based on the level of the BNP isoforms and other cardiac markers (p. 20, lines 25-26). Applicant further cites

Hybritech Inc. v. Monoclonal Antibodies, Inc. and *In re Wands* in support of the arguments. Applicant's arguments have been fully considered but they are persuasive.

In contrast, the specification fails to provide sufficient guidance as to how all the polypeptides comprising fragments and variants with at least 85% identity to a fragment of SEQ ID NO:1 are related to SEQ ID NO:3 or 36 that can be used as an diagnostic marker of heart failure. It is known in the art that transcription and translation of each gene are independent from each other. The specification fails to show that the transcription and translation of the claimed polypeptides and fragments are positively associated with SEQ ID NO:3 and 36.

The specification only discloses that an upregulated expression level of SEQ ID NO:3 and 36 is found in heart tissue from heart failure patients. However, the specification does not show that the claimed variant polypeptides or fragments are also upregulated and thus associated to the same disease or other diseases. The specification also fails to show that whether the claimed different variant polypeptides or fragments would act in the same manner as SEQ ID NO:3 and 36 in the patients suffering from heart failure.

Thus, it is also unpredictable whether all the claimed variant polypeptides or fragments are useful for a diagnostic marker of any diseases or other purposes since there is no guidance to indicate how the variant polypeptides or fragments are related to SEQ ID NO:3 or 36. It is unpredictable which, if any other variant polypeptides or fragments would be similarly upregulated, since the regulation is independent of the sequence of the protein. Since the specification fails to provide sufficient guidance as to

whether the variant polypeptides or fragments would be upregulated and whether they are related to heart diseases or other diseases, a skilled artisan cannot contemplate how to use the claimed variant polypeptides. Thus, a skilled artisan cannot contemplate how to use the claimed genus of polypeptides except SEQ ID NO:3 and 36.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, it is unpredictable what changes can be made and still maintain activity; and thus the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation. Note that

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03

9. Claims 1, 6-9 and 16 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record.

Claims 1, 6-9 and 16 as amended are directed to a purified polypeptide comprising an amino acid sequence selected from the group consisting of a) the amino acid sequence of SEQ ID NO:1, 3, or 36, b) as sequence having at least seven contiguous residues to the amino acid sequence of SEQ ID NO:1, c) a sequence having at least 85%-95% sequence identity to the amino acid sequence of SEQ ID NO:1 and d) a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length and a pharmaceutical composition comprising the claimed polypeptides.

On p.16-17 of the response, Applicant argues that amended claims meet the written description requirement and the specification shows Applicant's possession of the claimed polypeptides. Applicant argues that the specification teaches that BNP isoforms can be used to diagnose heart conditions and monitor treatment of heart conditions (p.3, lines 10-11 of the specification) and also teaches that the claimed polypeptides can function to stimulate cGMP production, vasoactivity and diuresis or natriuresis (p. 5-6 and examples 8-9 of the specification). Applicant further cites *Falko-Gunter Falkner v. Inglis* and *Ralston Purina Co. v. Far-Mar-Co., Inc.* in support of the arguments. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the specification only describes SEQ ID NOs: 3 and 36 and fails to teach the function of SEQ ID NO:1 or describe any other related proteins with limited homology. The specification fails to teach what specific common structures can or cannot be changed or included in the claimed polypeptide variants of SEQ ID NOs:1, 3

and 36 to preserve the activity of SEQ ID NOs:3 and 36 as in claim 1-c) and claims 6 and 8. In addition, the specification also fails to teach what common structures are required for the claimed polypeptides having an amino acid sequence b) at least seven contiguous residues to the amino acid sequence of SEQ ID NO:1, and d) a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length. Since the common characteristics/features of the isolated variant and fragment polypeptides are unknown, a skilled artisan can not envision the functional correlations of the genus with the claimed invention. Note that

"A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v.Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle &Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004)."

In contrast, the specification provides an invitation for others to discover a representative number of species, or to discover what constitutes any particular portion of the structure that must be conserved, with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. Thus, Applicant was not reasonably in possession of the "claimed genus of polypeptides". See MPEP 2163.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 7, 9 and 16 stand rejected under 35 U.S.C. 102(e) as being anticipated by U. S. Patent No. 6812339 (Venter et al., issued Nov 2, 2004, priority Sep 8, 2000, as in IDS). The rejection is maintained for the reasons made of record.

Claims 1, 7, 9 and 16 as amended are directed to a purified polypeptide comprising an amino acid sequence selected from the group consisting of a) the amino acid sequence of SEQ ID NO:1, 3, or 36, b) as sequence having at least seven contiguous residues to the amino acid sequence of SEQ ID NO:1, c) a sequence having at least 85%-95% sequence identity to the amino acid sequence of SEQ ID NO:1 and d) a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length and a pharmaceutical composition comprising the claimed polypeptides.

On p.18-19 of the response, Applicant argues that the sequence disclosed by the ‘339 patent does not teach "at least 85% identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length" as in instant claim 1. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the examiner asserts that the amino acid sequence of SEQ ID NO: 7086 disclosed by the ‘339 patent anticipates instant claims 1, 7, 9 and 16. In fact, the amino acid sequence of SEQ ID NO:7086 disclosed by the ‘339 patent comprises an

amino acid sequence (i.e. fragment) having at least 85% identity to a fragment of SEQ ID NO:1at least 7 contiguous residues in length as in claim 1-(d) because 85% of 7 residues (7x 0.85 (85%)) is equal to 5.95 residues. As previously made of record, SEQ ID NO:7086 of the '339 patent having 6 contiguous residues in length and 100% identical to a fragment of instant SEQ ID NO:1. Thus, the amino acid sequence of SEQ ID NO:7086 disclosed by the '339 patent meets the new limitation d) as recited in instant claims 1, 7, 9 and 16. Thus the '339 patent anticipates claims 1, 7, 9 and 16.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 1/5/09.

Claim Rejections - 35 USC § 112

11. Claims 1, 6-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1, 6-10 and 16 as amended are directed to a purified polypeptide comprising an amino acid sequence selected from the group consisting of a) the amino acid sequence of SEQ ID NO:1, 3, or 36, b) as sequence having at least seven contiguous residues to the amino acid sequence of SEQ ID NO:1, c) a sequence having at least 85%-95% sequence identity to the amino acid sequence of SEQ ID NO:1 and d)

a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length and a pharmaceutical composition comprising the claimed polypeptides.

The instant claims 1, 7 and 9 now recite new limitations of "at least seven contiguous residues" and "a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length", which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Although on p. 12 of the response, Applicant states that support for the claim amendment can be found at p. 8, lines 25-30. However, the examiner cannot find such support. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Accordingly, in the absence of sufficient recitation of the above new limitation, the specification does not provide adequate written description to support the limitation of "a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length" as recited in claim 1. Thus the above recitation constitutes new matter absent evidence for their support. Applicant is required to cancel the new matter in the reply to this office action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

Claim Rejections - 35 USC § 102

12. Claims 1, 7, 9 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by U. S. Patent No. 6887481 (Chan et al., issued May 3, 2005, priority Dec 16, 1998).

Claims 1, 7, 9 and 16 as amended are directed to a purified polypeptide comprising an amino acid sequence selected from the group consisting of a) the amino acid sequence of SEQ ID NO:1, 3, or 36, b) as sequence having at least seven contiguous residues to the amino acid sequence of SEQ ID NO:1, c) a sequence having at least 85%-95% sequence identity to the amino acid sequence of SEQ ID NO:1 and d) a sequence having at least 85% sequence identity to a fragment of SEQ ID NO:1 at least seven contiguous residues in length and a pharmaceutical composition comprising the claimed polypeptides.

U. S. Patent No. 6887481 (the '481 patent) teaches an isolated polypeptide comprising an amino acid sequence of SEQ ID NO:2, which meets the limitations of b) and d) as recited in instant claim 1. SEQ ID NO:2 disclosed by the '481 patent comprises an amino acid sequence (i.e. fragment) having at least 7 contiguous residues of SEQ ID NO:1 and having at least 85%-95% identity to a fragment of SEQ ID NO:1, which meets the limitations as recited in instant claims 1, 7, and 9 (see the sequence alignment below; col. 3, lines 19-24; col.7, lines 25-30 col. 52-53, claims 3 & 10, in particular). The '481 patent also teaches a composition comprising the claimed polypeptide in a compound or solution for injection, which meets the limitation of a pharmaceutical composition comprising the claimed polypeptide and a pharmaceutically

acceptable carrier as recited in instant claim 16 (see col. 18, line 45- col. 19, line 29, in particular). Thus, claims 1, 7, 9 and 16 are anticipated by U. S. Patent No. 6887481.

The sequence search results disclose as follows:

SEQ ID NO:1

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US-09-461-774-2
; Sequence 2, Application US/09461774
; Patent No. 6887481
; GENERAL INFORMATION:
;  APPLICANT: CHAN, Lily
;  APPLICANT: CHUNG, Maxey Ching Ming
;  APPLICANT: LIM, Renee Lay Hong
;  TITLE OF INVENTION: Bacterial-derived molecules and therapeutic and
;  TITLE OF INVENTION: diagnostic uses therefor
;  FILE REFERENCE: 1781-0180P
;  CURRENT APPLICATION NUMBER: US/09/461,774
;  CURRENT FILING DATE: 1999-12-15
;  NUMBER OF SEQ ID NOS: 22
;  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 2
;   LENGTH: 538
;   TYPE: PRT
;   ORGANISM: Mycobacterium tuberculosis
US-09-461-774-2

  Query Match             24.2%;  Score 8;  DB 2;  Length 538;
  Best Local Similarity   100.0%;  Pred. No. 9.5;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy         17 DTVRVTLG 24
              ||||||||
Db         23 DTVRVTLG 30
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Conclusion

13. NO CLAIM IS ALLOWED.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
May 28, 2009

/Christine J Saoud/
Primary Examiner, Art Unit 1647